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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/787,888	06/08/2001	Anders Pettersson	103364702US	9971

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EXAMINER
YOUNG, MICAH PAUL

ART UNIT	PAPER NUMBER
1615	13

DATE MAILED: 05/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/787,888	Applicant(s) PETTERSSON ET AL.	
	Examiner Micah-Paul Young	Art Unit 1615	

-- The MAILING DATE of this communication appears on the cover sheet with th correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 February 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Acknowledgment of Papers Received: Amendment/Response filed 2/26/03 and Terminal disclaimer filed 2/26/03.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

1. Claims 1- 21 rejected under 35 U.S.C. 103(a) as being unpatentable over Nyström (EP 0 324 725) in view Fine et al (Clinical Note, *Pain*, **45**, 1991, 149 – 153) and Stanley et al (USPN 5,288,497). Claims 1- 17 are drawn to pharmaceutical composition for the treatment of acute pain, sublingually. The composition is an ordered mixture of micro-particles that is free of water. The composition comprises carrier particles, which are coated to the surface of smaller active agent particles. The carrier comprises disintegrants, surfactants and other commonly used excipients all well known in the art. Claims 19 – 21 are drawn to a method of treating acute pain sublingually using the composition of the invention.

Nyström teaches essential elements of the claimed invention. The reference discloses an ordered mixture of drug particles in a carrier composition. The compound of the invention is water-free and includes comprises conventional pharmaceutical additives such as glidants, lubricants, surfactants, disintegrants, and other compounds well known in the art. The drug

particles of the invention measure no larger than 10 microns, while the carrier particles measure between 100 and 500 microns. The active agent is selected from various analgesic or anesthetic compounds known in the art, yet the specific compound is only restricted by its solubility in water, the lower the better. The most important aspect of the invention is the fact that the compound remains water-free so that the active agents do not dissolve too quickly. Also Nyström teaches various delivery methods, including oral and topical. The delivery method and specific location is non-critical as long as the composition remains water free (col. 2, lin. 43 – col. 5, lin. 14; Examples).

What is lacking in the reference is a disclosure of specific lubricants and active agents useful in the invention. The invention discloses the disintegrants, yet only suggests cellulose derivatives as the water-soluble polymers. The reference uses lactose and mannitol. Though is it well known in the art that such substances are natural polymers that are highly water-soluble. Stanley et al discloses a dissolvable matrix delivery system. The dissolvable matrix comprises natural polymers such as gelatins, lactose, and/or mannitol (col. 5, lin. 43-53; col. 6, lin. 3-17; col. 7, lin. 5-15). One of the active agents delivered by this system is fentanyl (col. 17, lin. 39-col. 20, lin. 23). Lubricants and other excipients are included in this formulation. These other excipient5s include bile acids and sodium lauryl sulfate (col. 16, lin. 50-63).

With regard to the active agent as claimed by applicant, fentanyl is well known in the art as an analgesic. As disclosed by Fine et al (Clinical Note, *Pain*, **45**, 1991, 149 – 153) oral transmucosal fentanyl citrate (OTFC) has been used in the art to deliver the analgesic sublingually. In the form of lollipops and lozenges, the OTFC has been delivered to patients suffering from acute breakthrough pain (Introduction).

With regard to claims 19 – 21 which recite a method for treating acute disorders using the composition of the invention. Though Nyström does not suggest the therapeutic effects of the composition, it is apparent that with the addition of analgesic or anesthetic compounds, the composition given its constituency and dissolution profile could be used to treat a range of disorders. Coupled with the knowledge in the art of OTFC, a skilled artisan would be able to use the invention of Nyström to deliver therapeutic agents to treat disorders acute or otherwise.

With regard to claims 5, 9 and 21, which recite specific concentrations and dosages for the composition constituents, these limitations are held as non-critical and obviated by the prior art. Nyström provides the general combination of active agent particles with bio/mucoadhesive particles, along with suggestions to specific excipients. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *In re Aller,* 220 F.2d 454 105 USPQ 233, 235 (CCPA 1955).

Furthermore the claims differ from the reference by reciting various concentrations of the active ingredient(s). However, the preparation of various pharmaceutical compositions having various amounts of the active is within the level of skill of one having ordinary skill in the art at the time of the invention. It has also been held that the mere selection of proportions and ranges is not patentable absent a showing of criticality. *In re Russell*, 439 F.2d 1228, 169 USPQ 426 (CCPA 1971).

With these aspects taken into consideration, one of ordinary skill in the art would have been motivated to combine the composition of Nyström along with its suggestions, with the knowledge in the art. A skilled practitioner would have been motivated by the suggestion of lubricants by Nyström, to combine the fentanyl and sodium lauryl sulfate of Stanley into the

formulation of Nyström. A skilled artisan would have been aware of the therapeutic properties of OTFC, and been motivated to include it into the composition as well. One of ordinary skill in the art would have been motivated to combine the teachings of Stanley with those of Nyström in order to provide analgesic properties to the composition and to provide sufficient lubrication though the use of the sodium lauryl sulfate. A skilled artisan also would have followed the teachings of Fine to discover the sublingual and transmucosal properties of fentanyl. It would have been obvious to one of ordinary skill in the art, at the time of the invention to combine these teachings with an expected result of an ordered mixture that is essential free of water and capable of delivering fentanyl to a patient in need, relieving whatever disorder is present.

Response to Arguments

2. Applicant's arguments filed 02/25/03 have been fully considered but they are not persuasive. Applicant argues that:

a. Nyström does not discloses bio/mucoadhesive agents

b. Nyström does not disclose all of the physical elements of the present invention or the sublingual administration of the invention

c. There is not motivation to combine the art of record

d. None of the references disclose the active agent as result-effective variables

3. With regard to arguments a. and b., it is the position of the Examiner that Nyström does in fact disclose and suggest the claimed invention. Nyström discloses an ordered mixture, which is free of water with carrier articles from 100 to 500 microns, within the limits of the invention. Nyström discloses an ordered mixture where the active agent particles are smaller than those of the carrier particles (24 microns), identical to that of applicant. The reference discloses carrier

particles where disintegrants are present within the particles and where the particles are granulated together during processing. These elements are all similar if not identical to those of applicant.

Also, in response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the physical state of the mucoadhesive agent; the way of admixing the agent; and the position of the agent within the composition) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

With regard to argument c., it is the position of the Examiner that sufficient motivation exists between the references. Nyström suggests various delivery methods for the composition of the invention (co. 4, lin. 55-col. 5, lin. 5). The reference stresses that the delivery method is unimportant as long as water is kept from the composition before the time of delivery. The reference suggests the inclusion of various other excipients such as flavourants and the like all well known in the art. The specific delivery method for the composition is irrelevant as long as the particle sizes are within certain parameters and the carriers are water-soluble. Stanley provides the suggestion of delivery and a proven technique for pain relief. Sublingual delivery of analgesics is well known and shown by the products of Stanley. Stanley and Nyström contain similar excipients specifically water soluble polymers (lactose, mannitol, gelatin, etc.). Stanley also provides the active agent fentanyl, which is well known as a treatment for break-through pain. This is shown in the teaching reference Fine. Fine established fentanyl history as a good

treatment of breakthrough of pain in cancer patients, and would provide motivation to a skilled artisan.

With regard to argument d., it can be seen by each reference that the delivery of the particular active or non-active agent would be in an amount sufficient to cause an effect. The disintegrant, and lubricant are both result-effecting components and are disclosed by the prior art combination. The disintegrants are established to be in concentration with the carrier particles and visa versa. The fentanyl is also a result-effective component since it determines the amount of analgesic relief. The carrier and disintegrants determine how the agent is released.

Applicant is invited to come forth with evidence to the criticality of the specific concentrations claimed. The Office does not have the facilities for examining and comparing applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same material structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed products are functionally different than those taught by the prior art and to establish patentable differences. *See Ex parte Phillips*, 28 U.S.P.Q.2d 1302, 1303 (PTO Bd. Pat. App. & Int. 1993), *Ex parte Gray*, 10 USPQ2d 1922, 1923 (PTO Bd. Pat. App. & Int.) and *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

Conclusion

4. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Micah-Paul Young whose telephone number is 703-308-7005. The examiner can normally be reached on M-F 7:30am-4:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on 703-308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are 703-746-7648 for regular communications and 703-746-7648 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1234.

Micah-Paul Young
Examiner
Art Unit 1615

MP Young
May 17, 2003

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600